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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,636	04/06/2005	Vladimir Petrovich Zavyalov	MINIFERON	9917

27772 7590 10/05/2007

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
10/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,636	ZAVYALOV ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/6/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The instant application, including amended specification and claims and preliminary amendment, was received on 4/6/2005 and has been entered into the record.

2. Claims 1-14 are currently pending and are the subject of this office action.

Information Disclosure Statement

The information disclosure statement received on 4/6/2005 has been considered by the Examiner. The Becquart reference has not been considered because it is not in English. Similarly, the Chertkova (2002) reference has been considered in view of the provided translation only, and the Chertkova (2003) and Aphasiazheva references have been considered only in view of the abstracts.

Claim Objections

1. Claim 1 is objected to for the following informalities: The Examiner suggests amending the phrase "containing" in claim 1 to either "comprising" or "consisting". For the purpose of examination, the Examiner has interpreted "containing" to mean "comprising". Furthermore, the Examiner suggests amending claim 1 to recite ".....amino acids selected from the top horizontal line.....". Claims 2-14 are object to for depending from objected claim 1.

2. The Examiner suggests amending the phrase "consisting essentially of" in claim 3 to either "comprising" or "consisting". For the purpose of examination, the term "consisting essentially of" has been interpreted to mean "comprising".

3. The Examiner suggests amending the phrase "has a sequences" in claim 6 to "comprises a sequence" or "consists of a sequence". For the purpose of examination, "has a sequence" has been interpreted to mean "comprises a sequence".

4. The Examiner suggests amending claim 6 to read "The fusion peptide" rather than "The fusionpeptide".

5. The Examiner suggest amending the phrase "drug composition" in claims 2, 4, 13, and 14 to "pharmaceutical composition". For the purpose of examination, "drug composition" has been interpreted to mean "pharmaceutical composition".

6. The Examiner suggest amending claims 7, 9, and 11-14 to remove the term "is according to" and replace with "consists of the amino acid sequence of SEQ ID NO" or "comprises the amino acid sequence of SEQ ID NO".

Specification

The specification is objected to for having sequences that are not identified by sequence identifier. When a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and a sequence identifier ("SEQ ID NO:X") must be used either in the drawing or in the Brief Description of the Drawings. See MPEP ' 2422.02. In the instant application, a sequence identifier must be used for the sequences appearing in Figure 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fusion peptide sequences consisting of the sequences of SEQ ID NO: 3 or SEQ ID NO: 4, does not reasonably provide enablement for any other peptide sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims

The claims of the instant invention are drawn to fusion peptide sequences comprising two peptides from interferon, wherein said peptides are bound with a linker consisting of at least one amino

acid residue, and further containing at least 10 amino acids selected from the table recited in claim 1. As written, the breadth of the claims is excessive because the claims read on any polypeptide comprising any two "fragments" of any interferon, linked by any potential linker as long as said linker is at least one amino acid, and further comprises any 10 amino acids from the table of claim 1. Furthermore, because "containing" can be interpreted as "comprising", the claimed fusion peptides can comprise any 10 amino acids from the table of claim 1, in any combination or in any position within the fusion peptide. Thus, the claims are drawn to a potentially very large number of peptides arising from a large number of potential combinations of any two interferon "fragments", any number of amino acids which could be considered a "linker", and then any combination of 10 amino acids selected according to the limitations for the table of claim 1.

The specification provides guidance and examples of the fusion peptides of SEQ ID NOs 3 and 4, and shows that the peptide of SEQ ID NO: 3 has retained IFN-α-like anti-viral activity. However, there is no guidance or examples showing any other fusion peptide that possesses any biological activity. Given the broadest reasonable interpretation, a "fragment" of an IFN can be as little as 1-2 amino acid residues. However, the is no guidance or examples that would show a person of ordinary skill in the art how to create any fusion peptide comprising two such fragments of an IFN, wherein said fragments are only 1-2 amino acids in length. There are also no functional limitations for the claimed fusion peptides recited in the claims, and thus the claims read on a potentially large number of potential peptides with no biological function. A skilled artisan would not be able to predict which of the many possible fragments from several possible interferons (IFN-γ, IFN-β, multiple types of IFN-α, for example) could be included with any 10 amino acids from the table of claim 1, in any order or position, and with all possible linker sequences, in order to create a fusion peptide with any biological activity, especially in view of the fact that the claims do not specify or recite any specific biological activity. Thus, one of ordinary skill in the art would require further, undue experimentation in order to make and then use any fusion peptide, other than SEQ ID NOs 3 and 4, that is commensurate with the full scope of claim 1. It is noted here that claims 2-14 are rejected for depending from claim 1.

2. Claims 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a "drug composition" comprising the fusion peptides of SEQ ID NO: 3 or SEQ ID NO: 4, wherein said "drug composition" is therapeutic for viral disorders, does not reasonably provide enablement for any other "drug composition" comprising any other peptide fusion, or therapeutic for any other disorder. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a "drug composition" comprising a fusion peptide of claim 1. Given the broadest reasonable interpretation, the claims read on a pharmaceutical composition comprising any fusion peptide, wherein said pharmaceutical composition can be used therapeutically for any disorder. The specification teaches that the fusion peptide of SEQ ID NO: 3 exhibits anti-viral activity in an invitro assay for inhibition of mouse encephalomiocarditis virus, but does not disclose any other activity associated with this peptide, nor anti-viral activity against other viruses. However, there is no other disclosed fusion peptide with any other biological activity, and as discussed above, one of ordinary skill in the art would require further, undue experimentation in order to make and use all such fusion peptides that are commensurate in scope with the limitations of claim 1. Thus, one of ordinary skill in the art would not know how to make and use any "drug composition" comprising any fusion peptide of claim 1, except for those of SEQ ID NO: 3 or 4, for therapeutic use for any disorder other than inhibition of murine encephalomiocarditis virus. A skilled artisan would thus also require further, undue experimentation in order to make and use all possible "drug compositions" for all possible disorders except viral disorders, wherein said drug composition comprises any peptide other than SEQ ID NO: 3 or 4.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to fusion peptides comprising any two "fragments" of any interferon, any linker as long as it comprises at least one amino acid, and any 10 amino acids from the table of claim 1, in any order or position. Although the specification describes the fusion peptides of SEQ ID NOs 3 and 4, these examples by themselves are not sufficient to impart adequate description of the claimed fusion peptides. The claims do not require the fusion peptides of the instant invention to have any biological activity, nor any particular structure other than comprising any two fragments of any interferon, any linker, and any 10 amino acids of the table of claim 1. Further, the specification does not provide adequate written description of which of the many possible interferon "fragments" could be used, or which regions or amino acids must be conserved in such fragments. The specification also does not teach

which of the many possible "linker" peptides could be used and still provide a functional fusion peptide with biological activity. Thus, the claims are drawn to a genus of fusion peptides that has not been adequately described in the specification.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that the claimed fusion peptides comprise any fragment of any interferon, and comprises any linker sequence, and any 10 amino acids from the table of claim 1. There is no identification of any particular portion of any interferon that must be conserved in order to maintain function. Furthermore, the claims do not specify that the at least 10 amino acids of the table of claim 1 be in any specific order or sequence, and thus the claims are drawn to any fusion peptide that comprises any 10 amino acids from the table, in any position within said fusion peptide. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only fusion peptides consisting of the amino acid sequences set forth in SEQ ID NO: 3 or 4, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first

paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-5 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Chertkova *et al* (Biopolimeri I klitiha, 2002, T. 18, Nr. 2, abstract and English translation submitted in the 4/6/2005 IDS). The claims of the instant invention are drawn to fusion peptide sequences comprising two peptides from inteferons, wherein said peptides are bound with a linker consisting of at least one amino acid residue, and further containing at least 10 amino acids selected from the table recited in claim 1. The claims further recite drug compositions comprising said fusion peptides, and fusion peptides further comprising a carrier protein, specifically albebetin, serum albumin, and immunoglobulin G, and fusion peptides wherein the interferon is human interferon α2.

Chertkova *et al* teaches a protein known as "albeferon", which is constructed by fusion of an interferon-a fragment consisting of the amino acids LKEKKYSP to the synthetic protein albebetin. Chertkova *et al* further discloses albeferon (i.e. LKEKKYSP-albebetin fusion) further fused to another interferon-a fragment, consisting of the amino acid residues LKDRHDF, wherein LKEKKYSP is fused at the N-terminus and LKDRHDF is also fused at the N-terminus, or alternatively, at the C-terminus. Thus, Chertkova *et al* teaches fusion peptides comprising two interferon fragments. These fragments comprise at least 10 amino acids selected from the table of claim 1 of the instant invention, and because the N-terminal-LKEKKYSP-albebetin-LKDRHDF-C-terminus fusion would have at least one amino acid selecting the two interferon fragments that could be considered a "linker", the disclosure of Cherkkova *et al* meets the limitations of claim 1. Furthermore, because the interferon fragments are from interferon-α, and the fragments are fused to the carrier protein albebetin, Chertkova *et al* also meets the limitations of claims 3, 5, and 10 of the instant invention. Finally, Chertkova *et al* discloses that these fusion peptides

exhibit anti-viral activity *in vitro*, and because the peptides would have been administered in a form suitable for administration to live cells (such as saline or another suitable buffer), the peptides were in some form of a "drug composition", thus meeting the limitations of claims 2 and 4.

2. Claims 1-5 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Dolgikh *et al* (Protein Engineering, 1996, Vol. 9, p. 195-200, submitted in the IDS received on 4/6/2005). The subject matter of the claims of the instant invention is discussed *supra*. Figure 1 of Dolgikh *et al* shows a fusion polypeptide comprising residues 131-138 of human interferon α2 fused to albebetin (see abstract and Fig. 1). Specifically, the amino acid sequence LKEKKYSP is fused to albebetin and are represented as residues 2-9 of the polypeptide shown in Fig. 1. These residues are recited in the table of claim 1 of the instant application, either on the top line, or in the case of the 2nd residue (K), as an acceptable substitute for a top line amino acid. Residues 12 (Gly, G) and 13 (Asp, D) of Fig. 1 of Dolgikh *et al* are also amino acids present on the top line of the claim 1 table or as one of the acceptable substitute amino acids. Thus, the sequence disclosed in Fig. 1 of Dolgikh *et al* comprises an interferon a2 fragment fused to albebetin. Because an interferon "fragment" can comprise any 1-2 amino acid fragment within an interferon, as discussed supra, the polypeptide of Dolgikh *et al* would also necessarily comprise a second interferon "fragment", selected from one of the remaining amino acid residues of Table 1. Furthermore, any amino acid(s) after the first interferon fragment could be considered as a "linker". Therefore, Dolgikh *et al* discloses a fusion protein comprising two interferon "fragments", a "linker", and at least 10 amino acids selected in accordance with the table of claim 1 (residues 2-9, 12, and 13 of Dolgikh), and thus meets the limitations of claim 1 of the instant application. Furthermore, because the fusion taught by Dolgikh *et al* further comprises the carrier protein albebetin, and the LKEKKYSP fragment is from interferon a2, Dolgikh *et al* also meets the limitations of claims 3, 5, and 10. Finally, Dolgikh *et al* discloses *in vitro* studies in which said fusion polypeptide was in a buffer comprising Tris-HCl and bacitracin, the limitations of claims 2 and 4 regarding "drug compositions" are also met.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can

normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert S. Landsman/
Primary Examiner, Art Unit 1647